FINAL REPORT

on

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INTEGRATED CHEMICAL AND MICROORGANISM MONITORING OF AIR USING GAS
CHROMATOGRAPHY/ION MOBILITY SPECTROMETRY: TOWARD AN EXPANDED-USE
VOLATILE ORGANIC ANALYZER (VOA)

by

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SUMMARY

The work described in this research program originated with
the choice by NASA of an ion mobility spectrometer for air
quality monitoring on-board the international spacestation.
Though the gas chromatograph-ion mobility spectrometer analyzer
known as VOA met or exceeded expectations, limitations in the
basic understanding of response and the utilization of
foundational principles into usable technology was considered
unacceptable. In this research program, a comprehensive model
for the origins of mobility spectra was proposed, tested and
verified. The principles considered responsible for the
appearance of mobility spectra have now been elucidated through
this project. This understanding has been applied in automated
identification of mobility spectra using neural networks and
routine procedures for this now exist. Finally, the limitation
on linear range has been shown to be a technical limitation and
not a fundamental limitation so that a hardware component was
crafted to extend the linear range of a mobility spectrometer by
10X. This project has led to one Ph.D. dissertation and one MS
thesis. In addition, over ten public presentations at
professional meetings and six journal publications have resulted
from this program of research. The findings are so plentiful
that total analysis of the findings may require four to six years
or more. The findings confirm that the decision to use VOA was
sound and that the chemical and physical principles of mobility
spectrometry are both understandable and predictable.

INTRODUCTION

The quality of air on-board spacecraft must be maintained
at a level sufficient to prevent sickness or impaired judgement
of inhabitants. In recirculated and enclosed atmospheres this
can be a daunting task in view of the possible excursions or
events that may occur uncontrolled in the spacecraft. The
accumulation of vapors that otherwise would be regarded as
harmless on earth is a concern as are those events which may be
considered emergencies; namely, on board electrical fires or
failed experiments that release chemicals into the atmosphere.
Approaches to monitoring air quality for volatile organic
compounds were narrowed in the early 1990s and in the mid-1990s,
the technology to meet the needs for the international space
station was selected and a program of development was begun.
This technology was based upon a gas chromatograph coupled to an
ion mobility spectrometer.

Gas chromatography has been an analytical measurement
technology since the early 1950s and is regarded as mature
technology and science (1). The advantages of GC in chemical
measurements is universally recognized as a useful or essential
component of analyzers of complex mixtures of organic compounds.
However, the gas chromatograph provides incomplete results that
make identification of chemicals problematic. Consequently,
detectors are used with gas chromatographs to provide the
additional information needed to identify and quantitatively
determine the components in mixtures. The range of prospective
detectors is vast and ranges from the most mature and refined
technology, mass spectrometry, to some optical based detectors
such as infrared spectrometers. An allied technology to mass
spectrometry is ion mobility spectrometry (IMS) which is
comparatively under-developed though some significant national
security applications exist for IMS (2). These include detection
of chemical weapons on the battlefield and the screening of hand-

held luggage for explosives in commercial aviation. The selection of an ion mobility spectrometer for use as a detector with a gas chromatograph inlet was made on the bases of cost, size, weight, and power in spite of its low level of development.

Throughout the mid- to late 1990s, a gas chromatograph-ion mobility spectrometer known as the volatile organic analyzer (VOA) was designed, prototyped, tested on earth, tested in space flight, and constructed in final form for the spacestation. Despite this impressive research and development program sponsored by NASA, little advancement was made in understanding some of the governing principles of IMS. This research program was conceived to bring IMS to a better level of development in three areas including data reduction, comprehension of spectral response and chemical structure, and overcoming the limitation in narrow linear range of response. Each of these was addressed as separate objectives over nearly 4 years. In the next section, these objectives are re-stated from the original proposal in the neighboring section afterwhich the accomplishments are described and discussed.

OBJECTIVES FROM THE RESEARCH PROJECT
(taken from the original proposal)

Overall Objective

The overall objective of our research program has been the creation of sophisticated analytical instruments suited for monitoring volatile organic compounds in air. A distinctive of our program is our interest in maintaining advanced capabilities with economies of size, weight, and power. In the last twelve years, the technology chosen for development has been ion mobility spectrometry which has undergone dramatic transformations for military communities worldwide to sense chemical agents in battlefield environments.

Project Objectives

In order to attain our goal of a highly capable, small, and lightweight air monitor, several specific objectives can be established and these are rooted in a few major limitations of IMS. These include:

Foundations of Artificial Intelligence or Automated Identifications

At the core of automated identifications is a reliable understanding of the response of an analyzer and confidence that response can be dependable for building libraries of spectra. Unfortunately, the ionization of molecules in air at atmospheric pressure is still incompletely understood, frustrating those seeking a reliable and well-characterized analytical method. Major emphasis must be given toward completing a broad model for atmospheric pressure chemical ionization (APCI) reactions with volatile organic compounds (VOCs). Another part of this portion of work will include the creation of a data base for VOCs with mobility spectra, minimum detection limits, and relative responses. The goal here is for a standard reference base developed in full awareness of the essential parameters of temperature and moisture as suggested from the studies on ionization chemistry. As part of an IMS data base, we will need to develop and apply a protocol for spectral processing. This involves much more than digital signal averaging or file format and includes decisions on whether spectra should be subjected to deconvolution algorithms as a standard procedure prior to entry into a data base. Questions of smoothing of data are also considerations that must be resolved not only to our satisfaction but to that of the greater IMS community. A final specific objective under the chemistry heading is a study of the effects of coeluting peaks on mobility spectra and the analytical implication of such unresolved vapor mixtures in IMS response and automated identification.

Hardware or Instrumentation

Although our laboratory is not inclined to enter the arena of instrument construction, we have the requisite skills to build prototype hardware when necessary. We will undertake some hardware development that is considered unavoidable to advance IMS technology. These few issues are the narrow linear range of IMS response, the configuration of GC/IMS packages, and the interfaces between analyzer and environment. One particular interest is in creating a servo inlet that automatically establishes mechanical gain or attenuation of chromatographic effluent without additional dead-volume or loss in chromatographic performance. Linear ranges of 10^4-10^5 are sought as our goal. In the issue of packaging, the major concern is the near-ambient temperature of the drift tube in the hand-held GC/IMS analyzers. For example, a hardware concern involves the need to operate IMS drift tubes at elevated temperatures for application to chemicals seen on spacecraft. We feel that temperatures of 125-150°C will be necessary for uncomplicated and reliable operation. Attention will be given to drift tube designs that require little power for heating and for creative application of heat to IMS drift tubes.

Software and Automated Identifications

Automated identification of chemicals using ion mobility spectra has been the single most limiting feature of contemporary activities in IMS worldwide. We have used the last year to establish brackets on procedures, approaches, quality of mobility spectra and more to position ourselves for a first attempt at automated identifications in IMS. Previous attempts have been military in nature with a limited test set. Thus, a primary objective is the realization and evaluation of an automated identification package. Further, our laboratory is engaged currently in creating a Windows environment package for GC/IMS and we will combine spectra preprocessing with neural networks

for automated identification of GC peaks as developed and described in the research plan. Presently, we have examined a small data base as a first iteration on discovering the tools needed to begin automated identifications. Naturally, a goal is to expand and refine these tentative exercises to bring to maturity this technology.

RESULTS AND DISCUSSION
(Accomplishments of the Research Program)

Foundations of Artificial Intelligence or Automated Identifications

The main theme in this section was to create an understanding of how mobility spectra are formed and what governs response of an ion mobility spectrometer at a molecular level. The first step was the creation of a comprehensive model to explain the behavior of ions in an IMS drift tube and the second step was the test of this model with selected experiments.

The model is based upon two principles:
A. ions are created in the ion source region under what may be considered steady-state conditions tending toward equilibrium so long as vapors of the sample and ions are present together and well-mixed.
B. ions that are withdrawn from the ion source region and placed into the clean gas region of the drift region, can undergo dissociations based upon ion stabilities with characteristic lifetimes. Only ions whose lifetimes exceed that of the drift time, will appear in the mobility spectrum. All other ions with short lives may undergo ionization in the source, but will not survive the transit to the detector and will not appear in the mobility spectrum. Moreover, cluster ions that are unstable will not survive and will not appear in the mobility spectrum.

C. thus, the chemistry that occurs in the ion source of an ion mobility spectrometer cannot be directly referenced to the mobility spectrum because of an intermediate step based upon kinetics of decomposition or dissociation that skews the ion intensities and even the existence of certain ions.

This concept or model was proposed at several international meetings of instrumentation scientists and was defended in a Ph.D. dissertation. Moreover, one manuscript has been published and another submitted for publication when this report was submitted.

These publications are:

Ewing, R.E., Stone, J.A.; Eiceman, G.A., "Heterogeneous Proton Bound Dimers in IMS, *International Journal of Mass Spectrometry* **1999**, in press.

Ewing, R.E.; Stone, J.A.; Eiceman, G.A. Nazarov, E.G.; Rodriguez, J.E., "Kinetics of Decomposition of Proton Bound Dimers of Alkyldimethylamines in Air at Ambient Pressure", *J. Physical Chemistry* **1999**, submitted.

Ewing, R.E., "Kinetic Decomposition of Proton Bound Dimer Ions with Substituted Amines in Ion Mobility Spectrometry", Ph.D. Dissertation, New Mexico State University, Las Cruces, NM 88003, December 1996.

Eiceman, G.A., Bergloff, J.F., Karpas, K. "Proton Abstraction and Association Reactions in Atmospheric Pressure Negative Chemical Ionization (APNCI) of Fluorinated Phenols", *Journal of American Mass Spectrometry,* **1999**, in press.

In the Ph.D. dissertation, a series of alkyl amines were examined to determine the validity of ion instability in the

drift region of the mobility spectrometer. The concept is that ions which undergo decomposition in the drift region can be understood in terms of enthalpy and entropy of association and that the kinetics of decomposition of proton bound dimers (an often used bit of information in mobility spectra of many compounds) can occur readily on the time scale near that of ion drift. For some chemicals such as alkyl amines, the decomposition occurs in less than 2 s at ambient temperature and pressure, though the ions can be stabilized with decreases in temperature. Within a chemical family such as alkyl amines, substitutions on the alkyl chain could cause instability so that entropy considerations became the governing influence. Thus, enthalpy alone did not explain which proton bound dimers of a given chemical were stable while a related but different chemical may not exhibit a proton bound dimer in its mobility spectrum. This was further clarified in the journal article submitted to J. Phys. Chem. (submitted July 1999).

In contrast to the alkyl amines, other chemicals such as ketones exhibit a stable proton bound dimer at temperatures up to and including 250°C. These chemicals apparently have enthalpy terms that reflect strong binding of the chemical to the proton core. Consequently, ketones and some others are stable to high temperature. At ambient temperature, a threshold for stability was found to be ~22 kcal mole^{-1} for the binding of molecules to a proton. In instances when this was exceeded by molecules in a proton bound dimer, the dimer was stable on drift tube time scales and was seen in the mobility spectrum. In instances when the enthalpy term was lower than 22 kcal mole^{-1}, the proton bound dimer did not appear in the mobility spectrum. Rather the ion decomposed in the drift region or even the ion source region near the ion shutters as the gas composition for the internal atmosphere became inhomogeneous through mixing of the drift gas with the sample vapor stream.

A limited amount of work was made using negative polarity chemicals and the ion chemistry was found to differ somewhat from

positive polarity insomuch as negative ions can undergo proton abstraction reactions. These were found to be influenced by temperature as were the dimer association ions such as M_2Cl^-.

Summary-For over 30 combinations of chemicals of heterogeneous proton bound dimers and for a few chemicals in great detail, the core concepts of the proposed model were validated and no evidence was found to disqualify the model. In short, a chemical must be ionized after which the ion must be sufficiently stable to traverse the drift region in order for a peak to appear in a mobility spectrum. Failure for a chemical to show response may mean that the chemical is not ionized or the ions are not sufficiently stable. Both of these are temperature dependent as described in the third section below. A model now exists in quantitative terms to allow a spectrum to be interpreted or predicted based upon known values for ΔH° and ΔS° or ΔG° for an ion in equilibrium with the sample neutral. The first objective in the original proposal was fulfilled and mobility spectra are now understandable with this model.

Hardware or Instrumentation

The essential purposes of the second objective were to create a high temperature IMS drift tube, couple that drift tube to a gas chromatograph, and explore means to increased the linear range of response in the IMS analyzer. After prolonged technical difficulties, a high temperature drift tube was crafted and details of this unit have been made known through oral presentations at professional meetings. The details of these high temperature drift tubes can be found in the thesis of Yuan-Feng Wang (see below). The interface between the IMS drift tube and a gas chromatograph was made facile and is also described in Wang's dissertation.

The core of this section was the creation of an extended linear range. In order to accomplish this, the principal

investigator visited the Univ. Manchester Institute of Science and Technology and made progress in a collaborative effort. The result was an extended linear range to about 100-500 versus ordinary 10-50 as shown in the following manuscript:

Young, D.; Thomas, C.L.P., Breach, J.; Brittain, A.H.; and Eiceman, G.A. "Extending the Concentration and Linear Dynamic Range of Ion Mobility Spectrometry with a Sheath Flow Inlet", 1998, Analytical Chimica Acta, 1999, 381(1), 69-83.

Summary-The procedures to construct high performance high temperature drift tubes in IMS have now been mastered and made known generally. In addition, a servo inlet was crafted to allow the linear range of response a 10-fold expansion. While this extension was useful somewhat in practical applications of IMS, the better use of these findings may be to clarify the difference between fundamental and technical limitations in IMS. Future and greater extensions of the linear range in response should be sought through other means. For example, a full use of all ions available to use in IMS may be a promising route of development. This would mean alternate source designs. This objective was fulfilled as planned though the anticipated increase in linear range was frustrated by high diffusion rates of gases. This limitation restricted the usefulness of a servo inlet device in IMS.

Software and Automated Identifications

        In this section, the original intention was to discover the means by which spectral identification might be made automated and this would involve both the creation of a large data base of mobility spectra and the integration of this into commercial or customized software. Previous attempts to created automated identifications for mobility spectra gave mixed results: some promising and some not so promising (3). Nonetheless, the available approach which was deemed best was that using neural

networks. The challenge was to discover what parameters in the mobility spectra and in the software would lead to optimum response.

The key to using neural networks with IMS data was discovered and was the need to have neural networks trained using spectra across a range of concentrations. Since spectra at various concentrations were available in a previous data base collected in the early 1990s, the software switches and procedures to make the networks successful were explored using that data base. The following manuscript describes this work and will have been published in 1999:

Bell, S.E.; Nazarov, E.G.; Wang, Y.F.; Eiceman, G.A., "Classification of Ion Mobility Spectra by Chemical Moiety Using Neural Networks with Whole Spectra at Various Concentrations", Analytica Chimica Acta **1999**, in press.

It was found that networks could attain better than 90% overall success when identifying chemicals that have been previously learned by the network and this was deemed very promising. The success with the data base noted above was tempered here since the spectra in that data base were obtained at low temperature and the VOA will be operated at 150°C. Since temperature is known to have an effect on mobility spectra, a new data base at elevated temperature needed to be created. Toward this end, a large data base of 162 volatile organic chemicals from sixteen chemical groups was created and this spanned five temperatures (150, 175, 200, 225, and 250°C) and three moistures (0.15, 2 and 200 ppm). Each chemical was entered to the IMS drift tube via a gas chromatograph so mobility spectra are available for each compound at 5-10 concentrations as proscribed by the chromatographic elution profile.

The creation of this data base has opened understanding and confirmation of origins of mobility spectra (see first objective

above) in a large and persuasive manner and the importance of
this work is summarized in the thesis of Yuan-Feng Wang

Yuan-Feng Wang, "Effects of Moisture and Temperature on Mobility
Spectra of Organic Chemicals", MS Thesis, New Mexico State
University, Las Cruces, NM June 1999.

Findings from this work have not been totally and
comprehensively analyzed and will continue to be explored during
the next five years (est.). The work is so large that detailed
studies will be continued well into the future using this data
base. Still, the following summary can be made:

Coefficients of reduced mobility, K_o, were influenced by
temperature and moisture suggesting varying levels of hydration
of ions in the drift tube. Certain chemical groups such as
aromatics and poly-aromatics were not influenced by temperature
since the product ions are known to be products of charge
exchange, M^+. In product ions where protonated monomers were
produced through proton transfer reactions, the influence of
moisture was pronounced. The K_o values decreased with increased
temperature, presumably as a hydrated ion underwent losses of
waters of hydration and the ion size decreased. All measurements
were made with reference to a chemical standard, 2,4-lutidine,
though findings here showed that 2,4-lutidine exhibited hydration
reactions, while organic-phosphates were less influenced by
moisture. Temperature exerted another influence on ion mobility
spectra, and several chemicals formed fragment ions at 250°C and
225°C. Other chemicals showed decomposition of proton bound
dimers and some showed both behaviors. Most chemicals exhibited
protonated monomers (MH^+) and proton bound dimers at 175°C and
150°C. However, 200°C seem a critical temperature, and the
spectra patterns of the product ions became very complex,
presumably through ion fragmentations. The changes in mobility
occur as $T^{0.5}$ for temperature alone. However, these results

suggest that changes in ion hydration shells are altering the identities of the ion clusters for the hydrated core ions. That is, as temperature is changed, the value for n in $H^+(H_2O)_n$ is undergoing changes. As temperature is increased, n is decreased. These findings have clarified the general patterns and trends of moisture and temperature for a large range of chemicals, but no interpretations are offered on the either mechanisms or pathways for ion-molecule chemistry.

As efforts are made to explore this data base, an understanding of the source of ion charge was considered essential and another study was prepared. This has been published as:

Eiceman,G.A.; Nazarov, E.G.; Rodriguez, J.E.; Bergloff, J.F. "Positive Reactant Ion Chemistry for Analytical, High Temperature Ion Mobility Spectrometry (IMS): Effects of Electric Field of the Drift Tube and Moisture, Temperature, and Flow of the Drift Gas", *International Journal of Ion Mobility Spectrometry* **1998**, 1, 36-45.

The findings from this work may be summarized here. The reactant ion peaks in positive polarity with a high temperature drift tube for ion mobility spectrometry were explored as a function of drift gas flow rate, temperature, and electric fields in certain regions of the drift tube. Changes that occurred in either the reduced mobilities or peak intensities could be understood in terms of known ion-molecule reactions or equilibria. Reactant ion peaks were sensitive to drift gas flow rates through a concentration dependence with material off-gassing. This may be governed by material sciences and drift tube constructed from materials different than those used here may have different characteristics. The use of high temperatures, it was hoped, would lessen the role of hydration of ions which can complicate IMS response at low temperatures. In these studies, it was found

that ion-molecule hydrations could be discerned even at 250°C and moistures of 0.1 ppm. Thermal expansion was found to affect drift tube dimensions sufficiently to alter calculated mobility constants and mobilities for a chemical standard (2,4-lutidine) obeyed the expected $K(T) \sim T^{0.5}$ when electric fields were corrected for thermal expansion. Elevated temperatures were found to diminish but not eliminate the subtle effects of moisture in the drift gas with respect to ion-hydration equilibria with the traditional reactant ion peaks. In any attempt to create a refined data base for high temperature mobility spectra, where standards are high for quantitative precision, attention must be given to drift tube parameters and in the absence of common drift tube designs or a reference-chemical based protocol, laboratory intercomparisions may be only approximate.

In summary-Mobility spectra have the properties to be crafted into automated identifications using commercial software (Neural Ware Pro II). In order to accomplish this, a large data base of mobility spectra was created and has produced a bountiful amount of detail about IMS response that can only be analyzed in the years to come.

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